

AMENDMENTS TO THE CLAIMS

1. **(Currently Amended)** A method for identifying a compound that binds to and/or modulates the activity of a Kv4.2 or Kv4.3 potassium channel by binding to and/or modulating the activity of a PCIP polypeptide comprising:

- a) contacting a 9q PCIP polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 14, 16, 18, 20, 22, 24, 26, and 28, or a cell expressing said 9q PCIP polypeptide, with a test compound; and
- b) determining whether said test compound binds to and/or modulates the activity of said 9q PCIP polypeptide, wherein said activity is selected from the group consisting of regulation of I_{to} currents, regulation of peak current amplitudes, regulation of current density, regulation of inactivation time constants, regulation of recovery from inactivation time constants, regulation of current activation threshold, regulation of the kinetics of inactivation, regulation of the repolarization of the membrane during an action potential, interaction with a potassium channel or portion thereof, modulation of neuronal excitability, modulation of action potential conduction, modulation of somatodendritic excitability, modulation of neurotransmitter release, regulation of the phosphorylation state of a potassium channel or portion thereof, binding to calcium, acting as a calcium dependent kinase, modulation of chromatin formation in a cell, modulation of vesicular traffic, modulation of protein transport in a cell, modulation of cytokine signaling in a cell, regulation of the association of a potassium channel or portion thereof with the cellular cytoskeleton, modulation of cellular proliferation, modulation of membrane excitability, influencing the resting potential of membranes, modulation of wave forms of action potentials, modulation of wave frequencies of action potentials and modulation of excitation thresholds, thereby identifying a compound that binds to and/or modulates the activity of a Kv4.2 or Kv4.3 potassium channel.

2. **(Currently Amended)** The method of claim 1, wherein the binding of said test compound to said 9q PCIP polypeptide, is detected by a method selected from the group consisting of:

- a) detection of binding by direct detection of test compound/polypeptide binding;
- b) detection of binding using a competition binding assay; and
- c) detection of binding using an assay for PCIP activity.

3. **(Currently Amended)** A method for identifying a compound that binds to and/or modulates the activity of a Kv4.2 or Kv4.3 potassium channel by binding to and/or modulating the activity of a PCIP polypeptide, comprising:

- a) incubating a cell expressing i) a potassium channel comprising a Kv4.3 or Kv4.2 subunit, or a fragment thereof that functions as a potassium channel and ii) a 9q PCIP polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 14, 16, 18, 20, 22, 24, 26, and 28, in the presence and absence of a test compound; and
- b) determining whether the test compound binds to/and or modulates the activity of said 9q PCIP polypeptide wherein said activity is selected from the group consisting of regulation of I_{to} currents, regulation of peak current amplitudes, regulation of current density, regulation of inactivation time constants, regulation of recovery from inactivation time constants, regulation of current activation threshold, regulation of the kinetics of inactivation, regulation of the repolarization of the membrane during an action potential, interaction with a potassium channel or portion thereof, modulation of neuronal excitability, modulation of action potential conduction, modulation of somatodendritic excitability, modulation of neurotransmitter release, regulation of the phosphorylation state of a potassium channel or portion thereof, binding to calcium, acting as a calcium dependent kinase, modulation of chromatin formation in a cell, modulation of vesicular traffic, modulation of protein transport in a cell, modulation of cytokine signaling in a cell, regulation of the association of a potassium channel or portion thereof with the cellular cytoskeleton, modulation of cellular proliferation, modulation of membrane excitability, influencing the resting potential of membranes, modulation of wave

forms of action potentials, modulation of wave frequencies of action potentials and modulation of excitation thresholds, thereby identifying a compound that binds to and/or modulates the activity of a Kv4.2 or Kv4.3 potassium channel.

4-10. **(Canceled)**

11. **(Previously Presented)** The method of any one of claims 1, 3, 17 or 19 wherein said compound is useful in treating a subject suffering from a cardiovascular disorder is associated with an abnormal I_{to} current.

12. **(Previously Presented)** The method of any one of claims 1, 3, 17 or 19, wherein said 9q PCIP is a human 9q.

13-14. **(Canceled)**

15. **(Previously Presented)** The method of any one of claims 1, 3, 17 or 19, wherein said compound is useful in treating a subject suffering from long-QT syndrome.

16. **(Previously Presented)** The method of any one of claims 1, 3, 17 or 19, wherein said compound is useful in treating a subject suffering from congestive heart failure.

17. **(Currently Amended)** A method for identifying a compound that binds to and/or modulates the activity of a Kv4.2 or Kv4.3 potassium channel by binding to and/or modulating the activity of a PCIP polypeptide, comprising:

- a) contacting a polypeptide comprising an EF domain, a Kv4.3 or Kv4.2 potassium channel α subunit binding domain, or a C-terminal core domain of a 9q PCIP polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 14, 16, 18, 20, 22, 24, 26, and 28, or a cell expressing said polypeptide, with a test compound; and
- b) determining whether said test compound binds to and/or modulates the activity of said polypeptide, wherein said activity is selected from the group consisting of regulation of I_{to} currents, regulation of peak current amplitudes, regulation of

current density, regulation of inactivation time constants, regulation of recovery from inactivation time constants, regulation of current activation threshold, regulation of the kinetics of inactivation, regulation of the repolarization of the membrane during an action potential, interaction with a potassium channel or portion thereof, modulation of neuronal excitability, modulation of action potential conduction, modulation of somatodendritic excitability, modulation of neurotransmitter release, regulation of the phosphorylation state of a potassium channel or portion thereof, binding to calcium, acting as a calcium dependent kinase, modulation of chromatin formation in a cell, modulation of vesicular traffic, modulation of protein transport in a cell, modulation of cytokine signaling in a cell, regulation of the association of a potassium channel or portion thereof with the cellular cytoskeleton, modulation of cellular proliferation, modulation of membrane excitability, influencing the resting potential of membranes, modulation of wave forms of action potentials, modulation of wave frequencies of action potentials and modulation of excitation thresholds, thereby identifying a compound that binds to and/or modulates the activity of a Kv4.2 or Kv4.3 potassium channel.

18. (Previously Presented) The method of claim 17, wherein the binding of said test compound to said biologically active fragment of said 9q PCIP polypeptide, is detected by a method selected from the group consisting of:

- a) detection of binding by direct detection of test compound/biologically active fragment binding;
- b) detection of binding using a competition binding assay; and
- c) detection of binding using an assay for PCIP activity.

19. (Previously Presented) A method for identifying a compound that binds to and/or modulates the activity of a Kv4.2 or Kv4.3 potassium channel, comprising:

- a) incubating a cell expressing i) a potassium channel comprising a Kv4.3 or Kv4.2 subunit, or a fragment thereof that functions as a potassium channel, and ii) a polypeptide

comprising an EF domain, a Kv4.3 or Kv4.2 potassium channel α subunit binding domain, or a C-terminal core domain of a 9q PCIP polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 14, 16, 18, 20, 22, 24, 26, and 28, in the presence and absence of a test compound; and

b) determining whether the test compound binds to and/or modulates the activity of said polypeptide, wherein said activity is selected from the group consisting of regulation of I_{to} currents, regulation of peak current amplitudes, regulation of current density, regulation of inactivation time constants, regulation of recovery from inactivation time constants, regulation of current activation threshold, regulation of the kinetics of inactivation, regulation of the repolarization of the membrane during an action potential, interaction with a potassium channel or portion thereof, modulation of neuronal excitability, modulation of action potential conduction, modulation of somatodendritic excitability, modulation of neurotransmitter release, regulation of the phosphorylation state of a potassium channel or portion thereof, binding to calcium, acting as a calcium dependent kinase, modulation of chromatin formation in a cell, modulation of vesicular traffic, modulation of protein transport in a cell, modulation of cytokine signaling in a cell, regulation of the association of a potassium channel or portion thereof with the cellular cytoskeleton, modulation of cellular proliferation, modulation of membrane excitability, influencing the resting potential of membranes, modulation of wave forms of action potentials, modulation of wave frequencies of action potentials and modulation of excitation thresholds, thereby identifying a compound that binds to and/or modulates the activity of a Kv4.2 or Kv4.3 potassium channel.

20-23. (Canceled)

24. (Previously Presented) The method of claim 17 or 19, wherein the EF domain is selected from the group consisting of:

- a) residues 116-127, 153-164, 189-200, or 237-248 of SEQ ID NO:14;
- b) residues 103-114, 140-151, 176-187, or 224-235 of SEQ ID NO:16;
- c) residues 116-127, 153-164, 189-200, or 237-248 of SEQ ID NO:18;
- d) residues 98-109, 135-146, 171-182, or 219-230 of SEQ ID NO:20;
- e) residues 98-109, 135-146, 171-182, or 219-230 of SEQ ID NO:22;

- f) residues 116-127, 103-114, 139-150, or 187-198 of SEQ ID NO:24;
- g) residues 66-77, 103-114, 189-200 or 237-248 of SEQ ID NO:26; and
- h) residues 98-109, 135-146, 171-182, or 219-230 of SEQ ID NO:28.

25. **(Currently Amended)** A method for identifying a compound that binds to and/or modulates the activity of a Kv4.2 or Kv4.3 potassium channel by binding to and/or modulating the activity of a PCIP polypeptide comprising:

- a) contacting a polypeptide that is at least 95% identical to a 9q PCIP polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 14, 16, 18, 20, 22, 24, 26, and 28 and retains the ability to bind to a Kv4 channel, or a cell expressing said polypeptide, with a test compound; and
- b) determining whether said test compound binds to and/or modulates the activity of said polypeptide, wherein said activity is selected from the group consisting of regulation of I_{K0} currents, regulation of peak current amplitudes, regulation of current density, regulation of inactivation time constants, regulation of recovery from inactivation time constants, regulation of current activation threshold, regulation of the kinetics of inactivation, regulation of the repolarization of the membrane during an action potential, interaction with a potassium channel or portion thereof, modulation of neuronal excitability, modulation of action potential conduction, modulation of somatodendritic excitability, modulation of neurotransmitter release, regulation of the phosphorylation state of a potassium channel or portion thereof, binding to calcium, acting as a calcium dependent kinase, modulation of chromatin formation in a cell, modulation of vesicular traffic, modulation of protein transport in a cell, modulation of cytokine signaling in a cell, regulation of the association of a potassium channel or portion thereof with the cellular cytoskeleton, modulation of cellular proliferation, modulation of membrane excitability, influencing the resting potential of membranes, modulation of wave forms of action potentials, modulation of wave frequencies of action potentials and modulation of excitation thresholds, thereby identifying a compound that binds to and/or modulates the activity of a Kv4.2 or Kv4.3 potassium channel.

26. **(Canceled)**